

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Strong, Peter
U.S. Appln. No. : 10/779,456
U.S. Filing Date : February 13, 2004
Title of Invention : CHITIN MICROPARTICLES AND THEIR MEDICAL USES
Confirm No. : 9496
Examiner : Kim, Yunsoo
Art Unit : 1644

745 Fifth Avenue
New York, NY 10151

FILED VIA EFS-WEB
ON FEBRUARY 5, 2008

DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Peter Strong, declare and state that:

1. I make this declaration in connection with U.S. application Serial No. 10/779,456. I am familiar with its prosecution history, particularly the Office Action mailed on October 5, 2007, as it pertains to the rejection under 35 U.S.C. §103(a) of claims 1-3, 5, 8, 9, 28-33, 35, and 36 as allegedly being unpatentable over Shibata *et al.* (J Immunol 164: 1314-21, 2000; hereinafter "Shibata") in view of Clinical Report (Pediatrics 100: 143-152, 1997) as evidenced by the specification of the present application, the Sigma Chitin powder product sheet, WO 97/20576 (hereinafter "the '576 publication"), Kim *et al.* (J Dent Child 71: 126-130, 2004; hereinafter "Kim"), and U.S. Patent No. 6,080,762 (hereinafter "the '762 patent").

2. I am a citizen of Great Britain. As indicated on my attached *Curriculum vitae*, I obtained a doctorate degree in Immunology from the University of Oxford and have been involved in a number of research areas, particularly related to allergies. I have served as the Chief Scientific

Officer and Director of CMP Therapeutics LTD., the assignee of this application, since 2004. In view of my education and experience, I consider myself to be an expert in the field to which this application pertains.

3. The claimed invention relates to a method of treating seasonal respiratory allergies, allergies to aeroallergens, or asthma in a patient comprising administering a therapeutically effective amount of a chitin microparticle (CMP) preparation intranasally or by inhalation to a patient in a therapeutically effective amount of between 0.01 and 100mg of CMP per kg of body weight. The CMPs have an average diameter of less than 10µm. According to the Examiner, Shibata relates to a method of treating an allergy caused by an aeroallergen such as ragweed, such that this method comprises administering CMP (N-acetyl-D-glucosamine) in saline (*e.g.*, a buffer). Shibata allegedly demonstrates that chitin administration provides prophylactic effects, causes ragweed desensitization, and induces Th1 cytokines which down regulate allergic airway inflammation. The Examiner relies on Clinical Report to allegedly show that nasal/intranasal administration is a well recognized route of delivering drugs in allergy treatment, and uses the specification of the present application and WO 97/20576 to allegedly show that insoluble chitosan is available for nasal administration. Further, the Examiner contends that the oral delivery dose of Shibata cannot be considered as a standard dose for intranasal delivery, uses the '762 patent to allegedly demonstrate that nasal or lung delivery has higher bioavailability as compared to oral delivery, and relies on Kim to show that a single oral dose of 0.7mg/kg is equivalent to an intranasal dose of 0.3mg/kg.

4. Contrary to the Examiner's assertion, one of ordinary skill in the art would not recognize that Shibata relates to a method of treating seasonal respiratory allergies, allergies to aeroallergens, or asthma. In Shibata, the mice used to test the CMP compositions were initially sensitized by intraperitoneal (i.p.) injection of ragweed allergen (see page 1315, left column). The purpose of the initial injections was to induce the allergy. The subsequent challenge to the mice was by intratracheal (i.t.) introduction of further ragweed allergen, which involves making a slit in the trachea and instilling allergen into the lungs – but notably **not** the upper respiratory tract or nasal passages – of the mouse. Hence, the challenge by i.t. introduction in Shibata only instills the lungs, although diseases like allergic rhinitis and asthma involve the upper respiratory tract as well as the lungs. Allergens do not bypass the upper tract as in Shibata's experiments. In fact, there is no indication in Shibata that orally administered CMP actually treats asthma, and at

most Shibata speculates that "oral administration of chitin may be a substitute for [such] bacterial exposure" (page 1320, right column).

5. In addition, the CMP composition in Shibata is administered orally and is not coupled or added to the initial i.p sensitization. The assumption in Shibata is that gut macrophages which contact the CMP migrate to the lungs of the mice, although there is no direct evidence in Shibata that substantiates this premise. Thus, all that is demonstrated in Shibata is that orally administered CMP down-regulates serum IgE and lung eosinophilia.

6. In contrast, the Examples in the application and the experiments described herein directly show that delivery of CMP by the claimed routes can treat seasonal respiratory allergies, allergies to aeroallergens, or asthma. Unlike in Shibata, these studies are more realistic since they involve stimulation of the entire nasal-pulmonary mucosa. For instance, the present application demonstrates that intranasal application of CMP was effective in down-regulating classic clinical physiological symptoms of allergic disease as measured by changes in airway hyper-responsiveness as well as indirect measurements such as serum IgE (see Example 5) and peripheral blood eosinophilia (see Example 1 and 2). This study used microgram quantities of CMP prepared by sonication of crab shell purified chitin powder obtained from Sigma Chemical Co. Analysis of the CMP revealed that the particles have a mean diameter of in the range of submicron up to 50 μ m, with 98% < 20 μ m. The application of CMP also induced an up-regulation of IL-12 and IFN γ , which are Th1-type cytokines with known anti-allergic effects, and a down-regulation of IL-4, which is one of the most potent Th2 cytokines in allergic disease (see Example 14). Treatment with CMP also inhibited the development of asthma in mice as indicated by a significant attenuation in airway hyperresponsiveness (see Example 12) which is a direct clinical assessment of allergic disease of the airways as prominent in asthma.

7. Furthermore, additional studies were conducted to test the efficacy of intranasally applied CMP as claimed against allergic disease induced by a broad range of clinically important aeroallergens including house dust mite, grass pollens, tree pollens, ragweed pollen as well as cat and dog dander allergens. The effect of treatment was assessed by whole body plethysmography to give a direct physiological measure of the asthmatic status of the lungs. In this technique, a transducer measures fluctuations in air pressure which is converted into a parameter called enhanced pause (Penh). Measurements are expressed as the % increase over baseline value.

Controls usually show an elevation of <100% above baseline, while asthmatic shows Penh that is >150% and severely asthmatic have Penh >200%.

8. In this study, mice were sensitized by i.p. injection of allergen extract in alum over 4 weeks. Mice were then challenged with allergen extract administered intranasally, and treated with a dose of 20-50 μ g (0.8mg/kg body weight) of CMP administered intranasally either 1-2 hours before or after allergen challenge. This challenge / treatment protocol was continued for a number of days until an asthmatic response was observed.

9. Intranasal Treatment with 20 μ g doses of CMP effectively abolished the development of asthmatic airway hyperresponsiveness induced by repeated allergen challenge with Bermuda grass pollen (see FIG. 1; $P < 0.0005$) and Timothy grass pollen (see FIG. 2; $P < 0.01$).

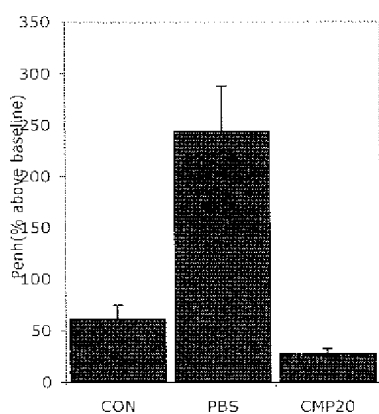


Figure 1

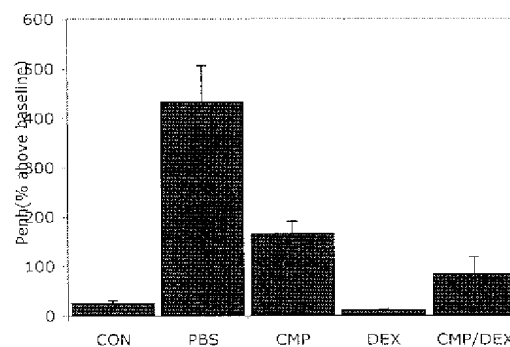


Figure 2

10. A group of allergic mice were also treated by injections of the corticosteroid dexamethasone (DEX) at an equivalent body weight dose used in humans. Intranasal Administration of CMP as claimed was as effective as the steroid drug in preventing asthma induced by Timothy grass pollen and suggests that the methods of the invention are capable of preventing the development of pulmonary allergic disease. When CMP-intranasally treated mice were given a large allergen challenge by Timothy grass pollen 24 hours after the last intranasal treatment with CMP, mice that had been treated with 20 μ g intranasal doses of CMP or injection with dexamethasone showed a 50% reduction in the asthmatic response (FIG. 3.).

11. Intranasal Treatment with 20µg doses of CMP was highly effective (see FIG. 4; $P < 0.005$) against ragweed-induced allergic disease and compared well to dexamethasone injections. Ragweed is the most important cause of allergic rhinitis in the US and Canada and approximately

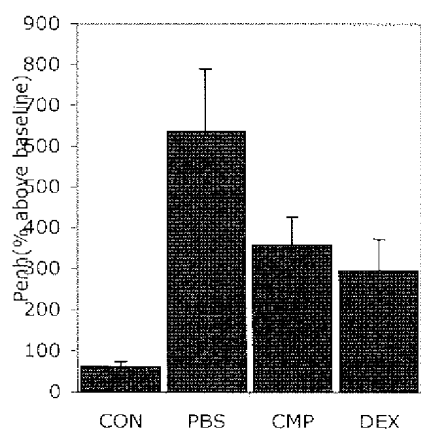


Figure 3.

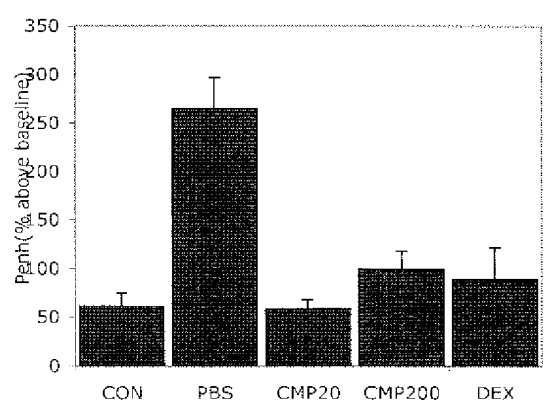


Figure 4.

75% of hay fever patients are allergic to ragweed. Comparison with a high dose treatment with 200µg of CMP given intranasally showed no significant advantage over the 20µg doses in reducing allergic airway hyper-responsiveness.

12. The methods of the present invention were tested against three common and important tree pollens: cedar pollen, birch pollen and oak pollen. Allergy to tree pollens accounts for about 30% of hay fever cases and one in four sufferers have allergies to both grass and tree pollens. Birch pollen seems to contain some of the most potent allergens such as Bet v 1 and in Europe more than 96% of tree pollen allergic sufferers are allergic to birch pollen. In Japan, allergy to cedar tree pollen is a public health issue affecting up to 20% of the population.

13. Intranasal Treatment with 20µg doses of CMP as claimed provided significant protection against development of airway hyperresponsiveness induced by cedar pollen (FIG. 5; $P < 0.01$) and birch pollen (FIG. 6; $P < 0.001$). As for oak pollen, treatment with 40µg of CMP significantly protected against the development of asthma (FIG. 7; $P < 0.005$) measured 24 hours after the allergen challenge.

14. The effects of intranasal treatment with CMP as claimed were also determined for cat and dog allergies. A treatment dose of 40 μ g (1.6mg/kg body weight) given intranasally was used. The CMP treatment reduced the onset of asthma provoked by the airway allergen challenge and was statistically very much lower on day 2 ($P<0.05$) and day 3 ($P<0.005$). Unlike treatment with

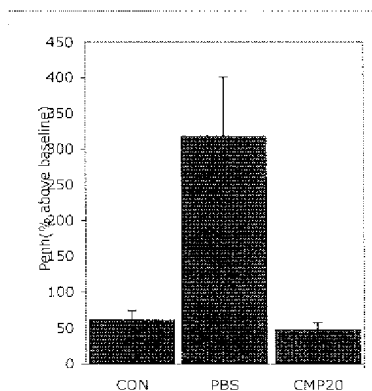


Figure 5

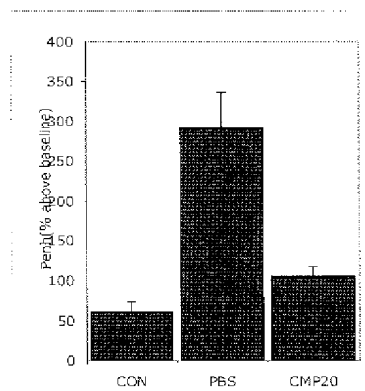


Figure 6

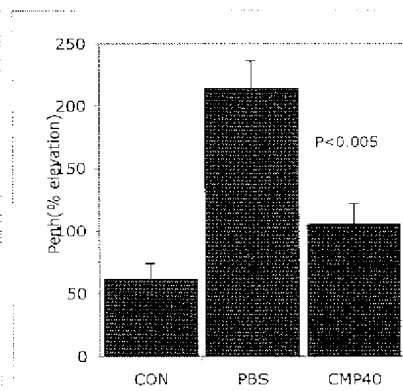


Figure 7

PBS saline, the intranasal CMP treatment seemed to progressively reduce the asthmatic status over time (FIG. 8).

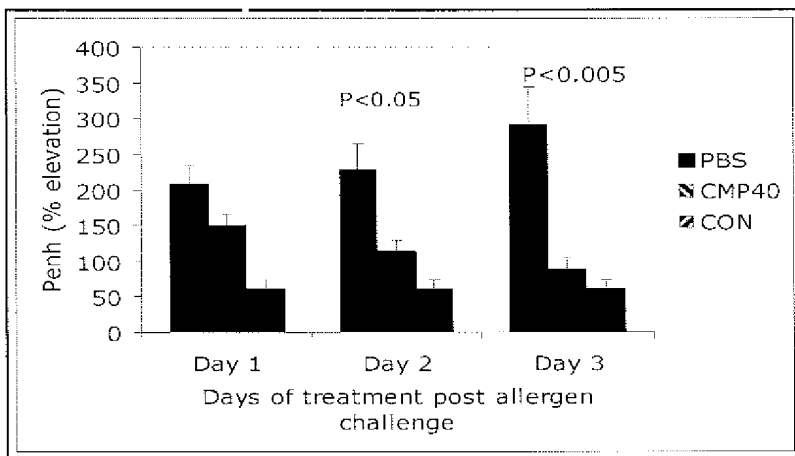


Figure 8

15. In the dog allergy study, mice were first made asthmatic by i.n. allergen challenge and then rested for 12 days before a further allergen challenge with or without treatment with 50 μ g CMP. Plethysmography was measured 24 hours later and revealed that intranasal CMP treatment as claimed reduced airway hyperresponsiveness by 32% and almost reached significance (FIG. 9; $P=0.058$).

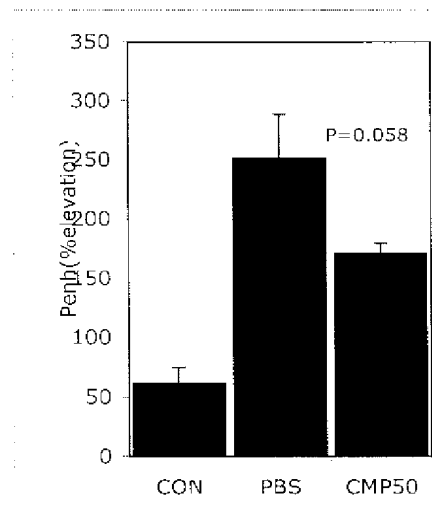


Figure 9

16. Together, these results demonstrate that the intranasal application of CMP as claimed is an effective prophylactic treatment for reducing the symptoms of allergic asthma produced in response to a broad range of common aeroallergens, including house dustmite, grass pollens, tree pollens, ragweed and animal dander. Importantly, Shibata does not show this and only implies that stimulation of Th1 cytokines by CMP would be beneficial for allergy, but the only direct physiological evidence provided is lung histology. Based upon Shibata's limited results, one skilled in the art would not presume that the methods of Shibata treat allergies as recited in the instant claims. Further, the skilled artisan would recognize that Clinical Reports does remedy the deficiencies in Shibata.

17. In addition, one skilled in the art would not apply the secondary references in support of the combination of Shibata and Clinical Reports. The secondary references relate to

"normal" types of drugs that are soluble and delivered systemically to the patient. Nasal delivery is useful for many drugs simply because the mucosa is thin and well-supplied with blood vessels. It is therefore a route that is sometimes useful for administering soluble drugs designed for systemic delivery to a site where the drugs are likely to be absorbed well via the blood vessels in the nose. This assertion is supported by the secondary references; for example, Kim relates to midazolam, which is a water-soluble drug, and indicates that intranasal delivery of midazolam has the potential advantage of rapid absorption (see page 126, left column). Also, the '762 patent relates to Raloxifene which is shown to be a soluble drug by the very fact that the efficacy of the delivery of Raloxifene was determined in the examples by measuring its concentration in blood samples from monkeys (column 7, lines 1-9) and by the explanation of the mechanism of intranasal delivery for soluble, systemically delivered drugs (column 7, lines 47-64).

18. In contrast to these normal drugs, CMP is not soluble, as indicated in the present specification (paragraph bridging pages 11 and 12) and in Shibata (page 1314, right column). The present invention also does not attempt to deliver CMP systemically, but to restrict it to the mucosa of the nose and upper respiratory tract where it acts topically, not systemically, improving immune function in these passages. Therefore, one skilled in the art would not apply the teachings of the secondary references to support the combination of Shibata and Clinical Reports.

19. Finally, one skilled in the art would consider the advantages of the present invention, which are not considered by the cited references. Firstly, the CMP composition of the present invention is formulated for delivery as a nasal spray, such that its immune modulating properties can be specifically directed to the site of allergic inflammation. As a result, the composition is much more effective for treating diseases of the nasal passages such as allergic rhinitis. Notably, there is no evidence from Shibata or Clinical Reports that indicates that oral delivery is effective for these conditions.

20. Also, there are safety advantages in using the claimed delivery routes of the present invention as compared to Shibata and Clinical Reports. If CMP produced an adverse reaction as it might in someone allergic to shrimp (generally used as a source of the CMP), then removing it after oral administration as used in Shibata and Clinical Reports would not be easy compared to nasal application, where the CMP could be removed by sneezing and irrigation.

21. Moreover, the present invention demonstrates greater efficiency of effect as compared to Shibata and Clinical Reports. Even assuming that the orally delivered CMP in Shibata did activate macrophages in the GI tract and a tiny fraction of these migrated to the nasal mucosa, the process would be inefficient as compared to the claimed routes of administration. In particular, in the absence of continual stimulation by proximity to CMP particles, the level of activation could not be maintained and the immune modulating effect in the nose would be short lived. Delivering CMP nasally ensures more robust and sustained activation of resident macrophages. It is clearly a more efficient process of activating nasal macrophages, which can then down-regulate asthma or allergic rhinitis. There is also concern of how the efficiency of the oral routes discussed in Shibata since nasal resident macrophages are more specialized for the nose and controlling immune status in the nasal mucosa, just as gut macrophages are specialized for immune status in the gut. Shibata and Clinical Reports do not even consider that oral routes would be less efficient for activating specific resident nasal macrophages as compared to intranasal routes.

22. In summary, the arguments presented herein demonstrate that one skilled in the art would not recognize that the present invention is obvious in view of the present invention. The skilled artisan would not consider that Shibata and Clinical Reports relates to a method of treating the allergies recited in the claims, nor would the skilled artisan consider that the teachings of the secondary references can be applied in support of Shibata and Clinical Reports. Further, one skilled in the art would recognize that the present invention has many advantages that are not considered or taught in the cited references. Therefore, I believe that the claimed invention is not obvious in consideration of the cited references.

23. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. These statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 1 February 2008

Peter Strong
Peter Strong

PETER STRONG, PhD

Home:
1 Kingsway Cottages
Bampton Road
Aston
Oxon OX18 2BT
UK

+44(0)1993 850852

Work:
CMP Therapeutics Ltd
Cherwell Innovation Centre
77 Heyford Park
Upper Heyford
Oxon OX25 5HD

+44(0)1869 238308

Email: pdmstrong@mac.com
Web site: <http://www.cmptherapeutics.com>

JOB REQUIREMENTS

Full time position with managerial responsibilities in Drug Development in the Pharmaceutical, Biotechnology or CRO sectors.

EDUCATION

PhD. Immunology. 2003. University of Oxford.
BSc(Hons) Biochemistry. 1976. University of Edinburgh.
Post Graduate Teaching Certificate in Secondary Education. 1977. University of Cambridge.

AWARDS

Medical Futures Innovation UK Award Competition finalist 2003.
Venturefest Business Plan Competition finalist 2002, 2003, 2004.
IP2IPO 2002 award for best technology innovation from the University of Oxford.

WORK EXPERIENCE

2004-present.

CMP Therapeutics Ltd
CEO: Bruce Savage
Cherwell Innovation Centre
77 Heyford Park
Upper Heyford
Oxon OX25 5HD.

Position: CHIEF SCIENTIFIC OFFICER, ACADEMIC FOUNDER AND DIRECTOR

Management of the development and commercialization of medical applications of chitin microparticles (CMP), an immune modulator delivered as a nasal spray for the prevention of allergy and viral infections (www.cmptherapeutics.com). Founded on IP generated by my research at the University of Oxford.

Responsibilities: Project Director and Project Manager

- Manufacturing Process Development
- Director of Pre-clinical development
- Director of Clinical Programs
- Management of CROs and Principle Investigators
- R&D Management: Academic collaborations
- IP Management: New patent filings. Translation of science into IP
- Management of Business Development: Commercialization strategy, market opportunities, presentation to investors

1994-2004.

MRC Immunochemistry Unit

Director: Professor K.B.M. Reid
Department of Biochemistry
University of Oxford
South Parks Road
Oxford OX1 3QU.

Position: Medical Research Scientist

Projects:

CMP project. This project was initiated and managed by myself and has been the main focus of my work at the ICU.

- 2000. Originated the concept of using chitin microparticles (CMP) to enhance macrophage activation and production of beneficial immune response in the respiratory mucosa.
- Identified potential commercial applications for treating allergies, respiratory infections and as a nasal vaccine adjuvant.
- Designed and executed experiments in mice to test the anti-allergic effects of CMP.
- Set up academic collaborations to test the anti-infective applications against bacterial pneumoniae.
- Set up collaborations with two groups in Japan to examine the adjuvant application in nasal vaccines against influenza and HIV. Results published in 2003 and 2005.
- Identified the market opportunity for developing a CMP-based nasal spray for treating / preventing hay fever.
- Designed and executed experiments to test the anti-allergic effect of CMP against grass, tree and ragweed pollen allergies. 2001.
- Initiated patent filing with the Medical research Council (MRC) using the support data generated by myself and by my collaborators.
- 2002. Published in Clin. Exp. Allergy.
- Began exploring the commercialization of my invention by entering the international Venturefest University of Oxford business plan competitions.
- Received the 2002 IP2IPO award for the best innovation from Oxford University and was selected as a finalist in the 2003 Medical Futures Innovation Awards and in the Venturefest Business Plan Competition in 2002 and 2003 and 2004.
- 2003. Presented at the UK Trade Consul to present CMP technology at a US biotechnology conference in San Francisco.
- Media presentations of my research through radio and newspapers and national television.
- Academic presentations of my research at scientific conferences.
- Initiated clinical collaborations and been instrumental in designing preliminary clinical trials in Europe.
- 2004. I founded CMP Therapeutics Ltd with the purpose of raising investment to develop the commercial applications of CMP for the treatment of allergies, respiratory infections and as an adjuvant in nasal vaccines (www.cmptherapeutics.com).
- Presented at investment forums as part of an ongoing process to attract investment into the company
- 2005. Trip to Japan to present CMP to local media and explore business opportunities

Recombinant hSP-D project.

- I contributed significant problem solving for developing novel methods for the expression and purification of rhSP-D in *E. coli*. This allowed significant advancement in the research activities of the Department.
- I initiated research into the therapeutic applications of rhSP-D for the treatment of allergy (Strong et al 2002 and 2003).
- I am co-inventor on an MRC patent filing for the application of rhSP-D in the treatment of chronic obstructive lung disease, allergy and infection.
- Method development for surfactant protein purification. I developed innovative methods for purifying SP-D and SP-A from human bronchoalveolar lavage and solved the problem of separating SP-D from SP-A (Strong et al 1998). This allowed significant advancement in the research activities of the Department.

Previous work experience.

1992-1994 Cortech, Inc.
6850 North Broadway
Denver, CO 80221

Position: Senior Research Associate in the Department of Immunological Chemistry.
Director: Dr. James Blodget, PhD.

Project: Development of dextran based bioconjugates for the suppression of sulphur drug allergies.
Synthesis of B and T cell peptides epitopes. Development of co-arrayed B and T cell epitope bioconjugates for a potential malaria vaccine.

1991-1992 Syntex Tech Center

2075 North St
Boulder CO 80303
Position: Research assistant / analytical chemist.
Project: Resolution of DL naproxen utilizing immobilized stereospecific enzymes.

1989-1990 Belle Bonfils Memorial Blood Center
Denver, CO
Position: Research assistant.
Project: R&D into new diagnostic immunological ELISA based assays for blood cell and serum antibodies for thrombocytopenia and leucocytopenia. Management of platelet antibody testing program, interaction with medical and technical personnel, report writing.

1988-1989 James P. Walsh & Associates
Environmental consultants
1002 Walnut St., Boulder, CO 80306
Position: Assistant analytical chemist.
Project: Detection of oil contamination in soil and ground water. Management of a mobile field lab utilizing gas chromatography analysis of soil samples.

1987-1988 University of Colorado
Boulder, CO
Position: Research assistant. Biochemistry.
Project: Synthesis and purification of self-cleaving RNA chains. Undergraduate tutoring.

1985-1986 Brighton Senior High School.
Brighton, CO
Position: Senior Chemistry Teacher.
Taught grades 9-12. Chemistry, General Science and Mathematics.

1984-1985 Colorado Academy
Denver, CO
Position: Senior Biology Teacher.
Taught 9th grade Biology. Designed a novel creative program for inquiry-based teaching.

1982-1984 University of Colorado
Boulder, CO
Position: Research assistant. Biochemistry.
Project: Angiotensin converting enzyme: extraction and purification. Study of active site geometry by inhibition kinetics of synthetic modified dipeptide inhibitors (Harris, Strong, Wilson. 1983).

1981-1982 Dawakin Kudu Science School
Nigeria, Africa
Position: Chemistry Teacher.
Taught grades 9 through 12. Helped develop a practical chemistry curriculum for a desert environment.

1979-1981 St. Aldates College
Oxford, England
Position: Head of Chemistry Department
Taught O and A level Chemistry. Chairman of the Staff Representative Committee.

1977-1979 Rossett High School
Harrogate, England
Position: Science Teacher
Taught O and A level Chemistry, CSE Biology and General Science.

WORK ETHOS:

- Pride in my creative problem solving skills.
- Resourceful and apply myself with considerable energy.
- Resilience and determination.
- Focused and always look to the end game and future purpose and direction for the project at hand.
- Entrepreneurial by nature and am most attracted to practical applications and the commercial process of translating ideas into marketable products.
- Global. I like to be involved in every step of the development process, from idea to plan implementation. Teamwork. My ideal is to establish teams to develop business opportunities.

- Personal. I am an easygoing person and enjoy working in a close-knit community. I am fascinated by small institution dynamics and I have many managerial concepts that I would like to put into action.

PERSONAL:

Male. Born 1 September 1954. UK citizen. Married to a US citizen. Two children. My wife is a US citizen, born in Colorado.

Interests include hiking, camping, skiing, traditional Irish music, folk dance and dance teaching, home brewing and gardening.

REFERENCES:

Bruce Savage
Cherwell Innovation Centre
77 Heyford Park
Upper Heyford
Oxon OX25 5HD
Email: bruce.savage@btinternet.com

Professor Kenneth Reid, PhD, FRS.
Medical Research Council Immunochemistry Unit
Department of Biochemistry
University of Oxford
South Parks Road
Oxford OX1 3QU
UK.
Email: kbr Reid@bioch.ox.ac.uk

Professor Henk Haagsman, PhD.
Faculty of Veterinary Medicine
P.O. Box 80.175
University of Utrecht
3508 TD Utrecht
The Netherlands.
Email: h.haagsman@vvd.vet.uu.nl

Selected Publications:

Strong, P., H. Clark, and K. Reid. 2002. Intranasal application of chitin microparticles down-regulates symptoms of allergic hypersensitivity to *Dermatophagoides pteronyssinus* and *Aspergillus fumigatus* in murine models of allergy. *Clin Exp Allergy* 32:1794-1800.

Ozdemir, Strong et al 2006. Treatment with chitin microparticles is protective against lung histopathology in a murine asthma model. *Clin Exp Allergy*. 2006 Jul;36(7):960-8.

Hamajima, K., Strong, P., et al. Chitin Micro-Particles (CMP): A Useful Adjuvant for Inducing Viral Specific Immunity when Delivered Intranasally with HIV-DNA Vaccine. *Viral Immunology* 16 (4), 2003.

Hasegawa, H., Strong, P., et al. Protection Against Influenza Virus Infection by Intranasal Administration of Hemagglutinin Vaccine With Chitin Microparticles as an Adjuvant. *J. Medical Virology*. 75:130-136 (2005).

Strong, P., Townsend, P., Mackay, R., Reid, K., Clark, H. 2003. A recombinant fragment of human SP-D reduces allergic responses in mice sensitized to house dust mite allergens. *Clin. Exp. Immunol* 134:181-187, 2003.

Strong, P., K. B. Reid, and H. Clark. 2002. Intranasal delivery of a truncated recombinant human SP-D is effective at down-regulating allergic hypersensitivity in mice sensitized to allergens of *Aspergillus fumigatus*. *Clin Exp Immunol* 130:19-24.

Shrive, A. K., H. A. Tharia, P. Strong, U. Kishore, I. Burns, P. J. Rizkallah, K. B. Reid, and T. J. Greenhough. 2003. High-resolution structural insights into ligand binding and immune cell recognition by human lung surfactant protein D. *J Mol Biol* 331:509.

Strong, P., U. Kishore, C. Morgan, A. Lopez Bernal, M. Singh, and K. B. Reid. 1998. A novel method of purifying lung surfactant proteins A and D from the lung lavage of alveolar proteinosis patients and from pooled amniotic fluid. *J Immunol Methods* 220:139-149.

Other Publications:

- Clark, H., N. Palaniyar, P. Strong, J. Edmondson, S. Hawgood, and K. B. Reid. 2002. Surfactant protein D reduces alveolar macrophage apoptosis in vivo. *J Immunol* 169:2892.
- Murray, E., W. Khamri, M. M. Walker, P. Eggleton, A. P. Moran, J. A. Ferris, S. Knapp, Q. N. Karim, M. Worku, P. Strong, K. B. Reid, and M. R. Thursz. 2002. Expression of surfactant protein D in the human gastric mucosa and during *Helicobacter pylori* infection. *Infect Immun* 70:1481.
- Madan, T., U. Kishore, M. Singh, P. Strong, E. M. Hussain, K. B. Reid, and P. U. Sarma. 2001. Protective role of lung surfactant protein D in a murine model of invasive pulmonary aspergillosis. *Infect Immun* 69:2728.
- Madan, T., U. Kishore, M. Singh, P. Strong, H. Clark, E. M. Hussain, K. B. Reid, and P. U. Sarma. 2001. Surfactant proteins A and D protect mice against pulmonary hypersensitivity induced by *Aspergillus fumigatus* antigens and allergens. *J Clin Invest* 107:467.
- Kishore, U., P. Strong, M. V. Perdikoulis, and K. B. Reid. 2001. A recombinant homotrimer, composed of the alpha helical neck region of human surfactant protein D and C1q B chain globular domain, is an inhibitor of the classical complement pathway. *J Immunol* 166:559.
- Wright, S. M., P. M. Hockey, G. Enhorning, P. Strong, K. B. Reid, S. T. Holgate, R. Djukanovic, and A. D. Postle. 2000. Altered airway surfactant phospholipid composition and reduced lung function in asthma. *J Appl Physiol* 89:1283.
- Kovacs, H., I. D. Campbell, P. Strong, S. Johnson, F. J. Ward, K. B. Reid, and P. Eggleton. 1998. Evidence that C1q binds specifically to CH2-like immunoglobulin gamma motifs present in the autoantigen calreticulin and interferes with complement activation. *Biochemistry* 37:17865.
- Kishore, U., L. E. Leigh, P. Eggleton, P. Strong, M. V. Perdikoulis, A. C. Willis, and K. B. Reid. 1998. Functional characterization of a recombinant form of the C-terminal, globular head region of the B-chain of human serum complement protein, C1q. *Biochem J* 333 (Pt 1):27.
- Leigh, L. E., B. Ghebrehiwet, T. P. Perera, I. N. Bird, P. Strong, U. Kishore, K. B. Reid, and P. Eggleton. 1998. C1q-mediated chemotaxis by human neutrophils: involvement of gC1qR and G-protein signalling mechanisms. *Biochem J* 330 (Pt 1):247.
- Madan, T., U. Kishore, A. Shah, P. Eggleton, P. Strong, J. Y. Wang, S. S. Aggrawal, P. U. Sarma, and K. B. Reid. 1997. Lung surfactant proteins A and D can inhibit specific IgE binding to the allergens of *Aspergillus fumigatus* and block allergen-induced histamine release from human basophils. *Clin Exp Immunol* 110:241.
- Madan, T., P. Eggleton, U. Kishore, P. Strong, S. S. Aggrawal, P. U. Sarma, and K. B. Reid. 1997. Binding of pulmonary surfactant proteins A and D to *Aspergillus fumigatus* conidia enhances phagocytosis and killing by human neutrophils and alveolar macrophages. *Infect Immun* 65:3171.
- Kishore, U., R. D. Sontheimer, K. N. Sastry, K. S. Zaner, E. G. Zappi, G. R. Hughes, M. A. Khamashta, P. Strong, K. B. Reid, and P. Eggleton. 1997. Release of calreticulin from neutrophils may alter C1q-mediated immune functions. *Biochem J* 322 (Pt 2):543.
- Wang, J. Y., U. Kishore, B. L. Lim, P. Strong, and K. B. Reid. 1996. Interaction of human lung surfactant proteins A and D with mite (*Dermatophagoides pteronyssinus*) allergens. *Clin Exp Immunol* 106:367.